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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,880	12/05/2003	Katsunari Tezuka	14539-005002 / JF-82US-C1	9815

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EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/729,880	TEZUKA ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 23-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/850,548.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/5/03;5/24/04;9/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks, filed on 02/07/2007, are acknowledged.

Claims 1 – 32 are pending.

2. Applicant's election of Group VII (claims 18 – 22, drawn to a method of treating graft versus host reaction or immune rejection accompanying transplantation comprising administering a composition comprising a substance having an activity in modulating signal transduction mediated by AILIM, wherein the substance is an antibody which binds to AILIM) in the reply filed on 02/-7/2007 is acknowledged.

Applicant further elected the Species of "graft versus host reaction."

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1 – 17 and 23 – 32 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 18 – 22 are under consideration in the instant application, as they read on the elected invention wherein the substance that modulates signal transduction by AILIM is an antibody which binds AILIM.

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies have been filed in parent Application USSN 09/850,548, filed on 06/12/2001.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

5. Claim 22 is objected to because it is directed to non-elected inventions.

6. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18 – 22 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the elected invention is limited to a method which utilizes an antibody that binds to AILIM or a portion thereof; however, the rejection is set forth with regard to the full scope of the generic claims as presently recited.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

A. The specification does not provide a sufficient enabling description of the claimed method, because it does not provide a sufficient enabling description of a "substance" that modulates signal transduction mediated by AILIM.

A person of skill in the art is not enabled to make and use any "substance" that modulates signal transduction mediated by AILIM, commensurate with the scope of the claims as presently recited, because it was well known in the art at the time the invention was made that molecules having highly diverse structural and biochemical properties can modulate signal transduction. Huang (Pharmacology and Therapeutics, 2000, 86: 201 – 215; see entire document) reviews e.g. on page 202 the daunting task faced by the skilled artisan in developing small molecule regulators of protein function, and notes that the process requires long periods of trial and error testing. The structure of such molecules cannot be readily determined by one of skill in the art based upon the guidance provided in the specification as-filed. Therefore, Applicant does not provide a sufficiently enabling disclosure regarding how to make and use the "substances" other than an antibody that binds to AILIM or a portion thereof, wherein the antibody has an activity in inhibiting proliferation of AILIM-expressing cells, or inhibiting production of interferon-γ or interleukin 4 by AILIM-expressing cells, as disclosed in the instant specification at page 27, lines 27 - 30.

B. The specification does not provide a sufficient enabling description of the claimed method as it relies on a substance that "modulates" signal transduction mediated by AILIM.

The term "modulation" encompasses two mutually exclusive directions of affecting signal transduction, upregulation and downregulation. A person of skill in the art at the time the invention was made was aware that if downregulation of AILIM-mediated signal transduction may contribute to treating transplant-related disorders, as disclosed in the instant specification, then upregulation of the same signal transduction pathway is likely to have the opposite effect, namely to exacerbate the condition. Therefore, one of skill in the art is not enabled to practice the claimed methods as they employ substances which upregulate signal transduction mediated by AILIM.

C. The specification does not provide a sufficient enabling description of the claimed method which comprises administering a generically recited "antibody" that binds to AILIM or a portion thereof.

The instant specification discloses at page 27, lines 27 – 30, that the antibodies of the invention have an activity in inhibiting proliferation of AILIM-expressing cells, or inhibiting production of interferon-γ or interleukin 4 by AILIM-expressing cells. However, one of skill in the art at the time the invention was made was aware that "an antibody that bind to AILIM" may upregulate, downregulate, or have no effect on signal transduction mediated by AILIM, and that only those antibodies which have the activities disclosed at page 27, lines 27 – 30 may be expected to be effective in the instantly claimed methods. Therefore, one of skill in the art is not enabled to practice the claimed method by administering the generically recited "antibody" that binds to AILIM or a portion thereof.

D. The specification does not provide a sufficient enabling description of the claimed method, because it does not provide a sufficient enabling description of the generically recited "AILIM."

The instant specification discloses at pages 17 – 18 that AILIM encompasses the respective polypeptides of human, rat, and mouse origin, as well as polypeptides having substantially the same amino acid sequence, such as having multiple amino acids, preferably 1 to10, substituted, deleted and/or modified, as long as the polypeptide has substantially the same biological properties. The disclosure that it is preferable that 1 to 10 amino acids be altered is not limiting, and therefore polypeptide variants with any number of amino acid substitutions, deletions, and/or modifications are within the scope of the recited "AILIM."

Applicant has disclosed three AILIM polypeptides, and thus has disclosed only three "variants". In the absence of some structural basis for the function that must be maintained by the members of the genus, the claimed invention is not described in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Further, even single amino acid differences can result in drastically altered functions between two costimulatory proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability, the skilled artisan would not reasonably expect a generically recited AILIM polypeptide having any number of amino acid substitutions, deletions, and/or modifications to share the same function as the native AILIM polypeptides human rat, or mouse origin, and there is insufficient guidance to direct the skilled artisan as to such functional sequences. Thus the recitation of "AILIM," when interpreted in light of the specification, does not allow the skilled artisan to make and use the functional polypeptide without undue experimentation, and therefore to practice the claimed methods.

8. The following is a quotation of the appropriate paragraphs of **35 U.S.C. 102** that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 18 – 22 are rejected under **35 U.S.C. 102(b)** as being anticipated by Kroczek (DE 198 21 060, laid open 04/15/1999), as evidenced by the Certified English translation (see entire document), and the definition of "AILIM" in the instant specification at page 17.

Kroczek teaches an antibody to the 8F4 polypeptide (see entire document).

The 8F4 polypeptide is a human AILIM polypeptide as evidenced by the definition of AILIM at page 17 of the instant specification.

Kroczek further teaches that antibodies to the 8F4 polypeptide can be used as pharmaceutical compositions to block the interaction of the 8F4 antigen with its receptor in methods of preventing rejection reactions in organ transplants (see e.g., page 12 of translation).

A blocking antibody to the 8F4 polypeptide is a protein that modulates signal transduction by AILIM, including proliferation and cytokine production, because Kroczek further teaches that the 8F4/AILIM polypeptide stimulates proliferation of T lymphocytes and enhances production of certain cytokines (see page 8 of translation). Although Kroczek does not specifically exemplify the inhibition of the cytokines interferon □ and interleukin 4 by antibodies to 8F4/AILIM, the individual cytokines inhibited would be inherent in any method comprising contacting AILIM/8F4 in vivo with a blocking antibody.

The reference teachings thus anticipate the instant claimed invention.

10. The **prior art made of record and not relied upon** is considered pertinent to applicant's disclosure: Coyle et al., US Pat. Pub. No. 2002/0164697 (of record: cited on IDS of 12/05/2003), earliest priority date – 10/07/1998. The reference appears to anticipate or make obvious the instant claimed invention.

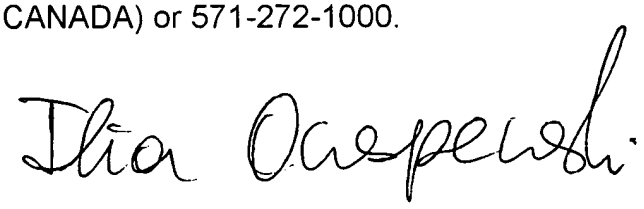
11. Conclusion: no claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ILIA OUSPENSKI, Ph.D.
Patent Examiner
Art Unit 1644



April 10, 2007